Claims:

A complete list of all claims under examination is set out below. Please cancel claims 1-10, 21, 23-25; 29, 30, 32 and 33; amend claims 11, 16, 19, 20, 22, 26-28 and 31, and add claims 34-43 as follows:

1-I0. (Cancelled)

11. (Amended) The compound of claim 34 claim 1 wherein the compound is represented by the formula:

$$R_{11}$$
 $(CH_2)_{\overline{m}}$
 R_{8}
 R_{25}
 R_{24}
 $(CH_2)_{y}$
 $(CH_2)_{y}$
 $(CH_2)_{x}$
 $(CH_2)_{x}$
 $(CH_3)_{x}$
 $(CH_$

wherein

 R_{11} is selected from the group consisting of C_5 - C_{12} alkyl, $\underline{C_5}$ - $\underline{C_{12}}$ alkoxy, C_5 - C_{12} alkenyl, and C_5 - C_{12} alkynyl;

 R_7 and R_8 are independently selected from the group consisting of O, S, CHR₂₆, CHR₂₆, NR₂₆, and N;

wherein R₂₆ is H, F or C₁-C₄ alkyl;

R₂₅ is N or CH;

R₂ is NH₂;

 R_3 is selected from the group consisting of H, C_1 - C_4 alkyl, $(C_1$ - C_4 alkyl)OH, and $(C_1$ - C_4 alkyl)NH₂;

R₁₅ is selected from the group consisting of hydroxy, phosphonate, and

2

wherein X and R_{12} are independently is selected from the group consisting of O and S;

 R_{23} is selected from the group consisting of H, F, OH, C_1 - C_4 alkyl, CO_2H and C_1 - C_4 alkyl;

R₂₄ is selected from the group consisting of H, F, C₁-C₄ alkyl and PO₃H₂, or R₂₃ together with R₂₄ and the carbon to which they are attached form a carbonyl group; and y and m are integers independently ranging from 0 to 4; or a pharmaceutically acceptable salt or tautomer thereof.

12. (Original) The compound of claim 11 wherein

m is 0;

y is 0 or 1;

R₂₅ is CH;

R₂₃ is H or F; and

 R_{24} is selected from the group consisting of H, F and C_1 - C_4 alkyl.

- 13. (Original) The compound of claim 11 wherein R₃ is selected from the group consisting of C₁-C₃ alkyl and (C₁-C₄ alkyl)OH.
- 14. (Original) The compound of claim 12 or 13 wherein

R₇ is NH; and

X is O;

or a pharmaceutically acceptable salt or tautomer thereof.

15. (Original) The compound of claim 14 wherein

y is 0; and

R₁₅ is OH.

16. (Amended) The compound of claim 13 wherein the compound is represented by the formula:

$$\begin{array}{c|c} & H \\ \hline \\ R_{11} \\ \hline \\ & R_{2} \\ \hline \\ & R_{3} \\ \\ & CH_{2})R_{15} \\ \\ & CH_{2})R_{15} \\ \\ & R_{11} \\ \hline \\ & R_{2} \\ \\ & R_{2} \\ \end{array}$$

wherein R_{11} is C_5 - C_{18} alkyl, C_5 - C_{12} alkoxy, or C_5 - C_{18} alkenyl; and R_8 is N; or a pharmaceutically acceptable salt or tautomer thereof.

17. (Original) The compound of claim 16 wherein R₁₅ is selected from the group consisting of hydroxy and

wherein R_{12} is O or S;

or a pharmaceutically acceptable salt or tautomer thereof.

(Original) The compound of claim 17 wherein R₁₁ is C₅-C₉ alkyl;
 R₁₅ is OH and

R₃ is selected from the group consisting of CH₃, CH₂CH₃, CH₂OH, CH₂CH₂OH and CH₂CH₂OH.

- 19. (Amended) A composition comprising a compound of claim [[1, 2, 6, 8]] 34, 11 or 16 and a pharmaceutically acceptable carrier.
- 20. (Amended) A <u>pharmaceutical</u> composition comprising a compound represented by the formula:

wherein R₁₁ is C₅-C₁₈ alkyl C₅-C₁₂ alkoxy or C₅-C₁₈ alkenyl;

Q is selected from the group consisting of C_3 - C_6 optionally substituted cycloalkyl, C_3 - C_6 optionally substituted heterocyclic, C_3 - C_6 optionally substituted aryl, C_3 - C_6 optionally substituted heteroaryl and -NH(CO)-;

[[R₂]] $\underline{R_3}$ is selected from the group consisting of H, C₁-C₄ alkyl and (C₁-C₄ alkyl)OH;

R₂₃ is H or C₁-C₄ alkyl, and

R₁₅ is selected from the group consisting of hydroxy, phosphonate, and

$$-x$$
 $-P$ OH

wherein X and R_{12} are independently is selected from the group consisting of O and S;

or a pharmaceutically acceptable salt or tautomer thereof and a pharmaceutically acceptable carrier.

- 21. (Cancelled)
- 22. (Amended) The composition of claim [[21]] $\underline{38}$ wherein R_{15} is selected from the group consisting of hydroxy and

wherein R₁₂ is O or S.

- 23. 25. (Cancelled)
- 26. (Amended) The method of <u>claim 36 elaim 25</u> further comprising the step of administering a second immuno-modulatory agent selected from the group consisting of cyclosporine, tacrolimus, rapamycin, azathioprine, and corticosteroids such as prednisolone and prednisone.
- 27. (Amended) The method of claim 36 elaim 25 wherein the compound has the general formula:

$$\begin{array}{c|c} H \\ N \\ \hline \\ R_8 \\ \hline \\ NH_2 \\ R_3 \\ \end{array}$$

wherein R_{11} is selected from the group consisting of C_1 - C_{22} alkyl, C_5 - C_{12} alkoxy, C_2 - C_{22} alkenyl and C_2 - C_{22} alkynyl;

 R_3 is selected from the group consisting of NH₂, OH, C₁-C₆ alkyl, (C₁-C₄ alkyl)OH, -(C₁-C₄ alkyl)NH₂, (C₁-C₄ alkyl)aryl(C₀-C₄ alkyl) and (C₁-C₄ alkyl)aryloxyaryl(C₀-C₄ alkyl);

R₈ is selected from the group consisting of O, S and N.

R₁₅ is selected from the group consisting of hydroxy, phosphonate, and

$$-x-P$$
OH:

wherein R₁₂ is selected from the group consisting of O, NH and S; and X is selected from the group consisting of O, NH and S; or a pharmaceutically acceptable salt or tautomer thereof.

28. (Amended) A method of promoting wound healing in a warm blooded vertebrate, said.

method comprising the step of administering a composition comprising a [[a]] compound of the general structure:

$$R_{11}$$
 Q R_{23} R_{15} R_{15}

wherein R₁₁ is C₅-C₁₈ alkyl, C₅-C₁₂ alkoxy, or C₅-C₁₈ alkenyl;

3 A: .

Q is selected from the group consisting of C_3 - C_6 optionally substituted cycloalkyl, C_3 - C_6 optionally substituted heterocyclic, C_3 - C_6 optionally substituted aryl, C_3 - C_6 optionally substituted heteroaryl and -NH(CO)-;

[[R₂]] \underline{R}_3 is selected from the group consisting of H, C₁-C₄ alkyl and (C₁-C₄ alkyl)OH;

R₂₃ is H or C₁-C₄ alkyl, and

R₁₅ is selected from the group consisting of hydroxy, phosphonate, and

$$-x$$
 $-P$ OH OH

wherein X and R_{12} are independently is selected from the group consisting of O and S;

or a pharmaceutically acceptable salt or tautomer thereof.

- 29. (Cancelled)
- 30. (Cancelled)
- 31. (Amended) A method for treating a patient suffering from a disease associated with abnormal cell growth, said method comprising the steps of administering a [[a]] compound of the general structure:

wherein R_{11} is located in the meta or para position and is selected from the group consisting of C_5 - C_{18} alkyl and C_5 - C_{18} alkenyl;

Q is selected from the group consisting of C_3 - C_6 optionally substituted cycloalkyl, C_3 - C_6 optionally substituted heterocyclic, C_3 - C_6 optionally substituted aryl C_3 - C_6 optionally substituted heteroaryl and -NH(CO)-;

 $\underline{R_3}$ [[$\underline{R_2}$]] is selected from the group consisting of H, C_1 - C_4 alkyl and (C_1 - C_4 alkyl)OH;

R₂₃ is H or C₁-C₄ alkyl, and

R₁₅ is selected from the group consisting of hydroxy, phosphonate, and

wherein X and R_{12} are independently is selected from the group consisting of O and S;

or a pharmaceutically acceptable salt or tautomer thereof.

- 32. (Cancelled)
- 33. (Cancelled)
- 34. (New) A compound represented by the formula:

wherein

 R_{11} is selected from the group consisting of C_5 - C_{12} alkyl, C_5 - C_{12} alkenyl, C_5 - C_{12} alkynyl, C_5 - C_{12} alkoxy, $(CH_2)_pO(CH_2)_q$, C_5 - C_{10} (aryl) R_{20} , C_5 - C_{10} (heteroaryl) R_{20} , C_5 - C_{10} alkoxy(aryl) R_{20} , C_5 - C_{10} alkoxy(heteroaryl) R_{20} and C_5 - C_{10} alkoxy(cycloalkyl) R_{20} ;

wherein R₂₀ is H or C₁-C₁₀ alkyl;

R₂₉ is H or halo;

R₂ is NH₂;

. R_3 is selected from the group consisting of H, C_1 - C_6 alkyl, $(C_1$ - C_4 alkyl)OH, and $(C_1$ - C_4 alkyl)NH₂;

R₂₃ is selected from the group consisting of H, F, NH₂, OH, CO₂H, C₁-C₆ alkyl, (C₁-C₄ alkyl)OH, and (C₁-C₄ alkyl)NH₂;

R₂₄ is selected from the group consisting of H, F and PO₃H₂, or R₂₃ together with R₂₄ and the carbon to which they are attached form a carbonyl group;

 R_{25} , R_7 , and R_8 are independently selected from the group consisting of O, S, CHR₂₆, CR₂₆, NR₂₆, and N;

wherein R_{26} is H, F or C_1 - C_4 alkyl;

R₁₅ is selected from the group consisting of hydroxy, phosphonate, and

wherein R_{12} is selected from the group consisting of O, NH and S;

X is selected from the group consisting of O, NH and S;

y and m are integers independently ranging from 0 to 4;

p and q are integers independently ranging from 1 to 10;

or a pharmaceutically acceptable salt or tautomer thereof.

35. (New) A method for modulating the activity of an S1P receptor, said method comprising contacting said receptor with a compound represented by the formula:

wherein

 R_{11} is selected from the group consisting of C_1 - C_{12} alkyl, C_2 - C_{12} alkenyl, C_2 - C_{12} alkynyl, C_5 - C_{12} alkoxy, $(CH_2)_pO(CH_2)_q$, C_5 - C_{10} (aryl) R_{20} , C_5 - C_{10} (heteroaryl) R_{20} , C_5 - C_{10} alkoxy(aryl) R_{20} , C_5 - C_{10} alkoxy(heteroaryl) R_{20} and C_5 - C_{10} alkoxy(cycloalkyl) R_{20} ;

wherein R₂₀ is H or C₁-C₁₀ alkyl;

R₂₉ is H or halo;

R₂ is NH₂;

 R_3 is selected from the group consisting of H, C_1 - C_6 alkyl, $(C_1$ - C_4 alkyl)OH, and $(C_1$ - C_4 alkyl)NH₂;

R₂₃ is selected from the group consisting of H, F, CO₂H, OH, C₁-C₆ alkyl, (C₁-C₄ alkyl)OH, and (C₁-C₄ alkyl)NH₂;

 R_{24} is selected from the group consisting of H, F and PO_3H_2 , or R_{23} together with R_{24} and the carbon to which they are attached form a carbonyl group;

R₂₅, R₇ and R₈ are independently selected from the group consisting of O, S, CHR₂₆, CR₂₆, NR₂₆, and N;

wherein R₂₆ is H, F or C₁-C₄ alkyl;

R₁₅ is selected from the group consisting of hydroxy, phosphonate, and

wherein R₁₂ is selected from the group consisting of O, NH and S;

X is selected from the group consisting of O, NH and S;

y and m are integers independently ranging from 0 to 4;

p and q are integers independently ranging from 1 to 10;

or a pharmaceutically acceptable salt or tautomer thereof.

36. (New) A method of providing immuno-modulation to a patient in need thereof, said method comprising the step of administering to said patient a composition comprising a compound represented by the formula:

wherein

 R_{11} is selected from the group consisting of C_1 - C_{18} alkyl, C_2 - C_{18} alkenyl, C_2 - C_{18} alkynyl, C_5 - C_{18} alkoxy, $(CH_2)_pO(CH_2)_q$, C_5 - C_{10} (aryl) R_{20} , C_5 - C_{10} (heteroaryl) R_{20} , C_5 - C_{10} (cycloalkyl) R_{20} , C_5 - C_{10} alkoxy(aryl) R_{20} , C_5 - C_{10} alkoxy(cycloalkyl) R_{20} ;

wherein R₂₀ is H or C₁-C₁₀ alkyl;

R₂₉ is H or halo;

R₂ is NH₂;

 R_3 is selected from the group consisting of H, C_1 - C_6 alkyl, $(C_1$ - C_4 alkyl)OH, and $(C_1$ - C_4 alkyl)NH₂;

R₂₄ is selected from the group consisting of H, F and PO₃H₂, or R₂₃ together with R₂₄ and the carbon to which they are attached form a carbonyl group;

 R_{25} , R_7 and R_8 are independently selected from the group consisting of O, S, CHR₂₆, CR₂₆, NR₂₆, and N;

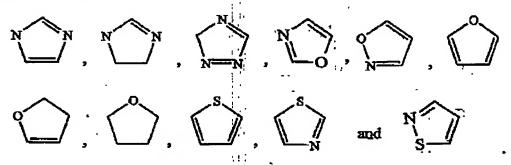
wherein R₂₆ is H, F or C₁-C₄ alkyl;

R₁₅ is selected from the group consisting of hydroxy, phosphonate, and

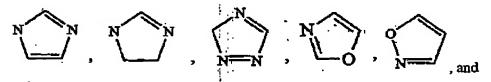
wherein R₁₂ is selected from the group consisting of O, NH and S;

X is selected from the group consisting of O, NH and S; y and m are integers independently ranging from 0 to 4; p and q are integers independently ranging from 1 to 10; or a pharmaceutically acceptable salt or tautomer thereof.

- 37. (New) The method of claim 26 wherein the corticosteroids is prednisolone or prednisone.
- 38. (New) The composition of claim 20 wherein Q is selected from the group consisting of



39. (New) The composition of claim 22 wherein Q is selected from the group consisting of



R₁₅ is OH;

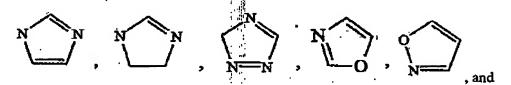
or a pharmaceutically acceptable salt or tautomer thereof.

40. (New) The method of claim 28 wherein Q is selected from the group consisting of NH(CO)-,

and R₁₅ is selected from the group consisting of hydroxy and

wherein R_{12} is O or S.

41. (New) The method of claim 40 wherein Q is selected from the group consisting of



R₁₅ is OH;

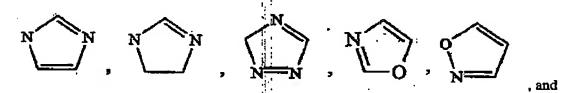
or a pharmaceutically acceptable salt or tautomer thereof.

42. (New) The method of claim 31 wherein Q is selected from the group consisting of - NH(CO)-;

and R₁₅ is selected from the group consisting of hydroxy and

wherein R_{12} is O or S.

43. (New) The method of claim 42 wherein Q is selected from the group consisting of



R₁₅ is OH;

or a pharmaceutically acceptable salt or tautomer thereof.

This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

BLACK BORDERS

IMAGE CUT OFF AT TOP, BOTTOM OR SIDES

FADED TEXT OR DRAWING

BLURRED OR ILLEGIBLE TEXT OR DRAWING

SKEWED/SLANTED IMAGES

COLOR OR BLACK AND WHITE PHOTOGRAPHS

GRAY SCALE DOCUMENTS

LINES OR MARKS ON ORIGINAL DOCUMENT

REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY

IMAGES ARE BEST AVAILABLE COPY.

OTHER:

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.